REMARKS

1. Introduction

In the Office Action mailed September 10, 2004, the Examiner rejected claims 1-4 and 8 under 35 U.S.C. 103(a) as being unpatentable over Nasir et al., *Combinatorial Chemistry & High Throughput Screening* ("Nasir") in view of Dixon et al., U.S. Patent No. 4,835,100 ("Dixon") and further in view of Dhar et al., U.S. Pub. No. 2002/0110803 ("Dhar"). The Examiner rejected claims 5-7 under 35 U.S.C. 103(a) as being unpatentable over Nasir, in view of Dixon and further in view of Dhar and further in view of Michel et al., U.S. Patent No. 5,741,654 ("Michel"). The Examiner rejected claims 9-10 under 35 U.S.C. 103(a) as being unpatentable over Nasir, in view of Dixon and further in view of Dhar and further in view of McMahon et al., U.S. Patent No. 5,166,078 ("McMahon"). The Examiner rejected claims 11-18 as being unpatentable over Nasir, in view of Dhar and further in view of Dixon.

For the reasons set forth below, Applicants respectfully request reconsideration and allowance of the claims.

2. Interview

Applicants thank the Examiner for scheduling the telephonic interview conducted on December 8, 2004. The interview was attended by Richard A. Machonkin, on behalf of Applicants, and by Examiners Long V. Le and Deborah A. Davis. The pending claims and the prior art, particularly the Nasir and Dhar references were discussed. The general thrust of the arguments presented to the Examiners was that the prior art of record would not have motivated one of ordinary skill in the art to derivatize aflatoxin to form an aflatoxin oxime and then to conjugate the aflatoxin oxime with a flourophore to provide a fluorescent tracer for a

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fluorescence polarization assay, nor did the prior teach that such a tracer would have the special property of being able to bind to an antibody to produce a detectable change in fluorescence polarization. However, no agreement was reached.

3. Response to Claim Rejections

a. Other Flourescence Polarization Applications

As noted during the interview, Applicants have filed two other applications directed to fluorescence polarization assays for mycotoxins that have now issued as patents. U.S. Patent No. 6,482,601 is directed to a fluorescence polarization assay for fumonisin, and U.S. Patent No. 6,812,036 is directed to a fluorescence polarization assay for deoxynivalenol. The latter patent was examined by the same two Examiners involved in the interview for the present application. Applicants respectfully submit that these two issued cases provide useful background information regarding fluorescence polarization assays and support the patentability of the present invention.

b. No Motivation To Combine The Cited References

The Examiner's rejections of the claims under § 103 is premised on a combination of three references: Nasir, Dixon, and Dhar. However, in order for this combination to establish a *prima facie* case of obviousness, the prior art must also provide a suggestion or motivation to make this combination. *See* MPEP § 2143.01. Thus, "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." *See* MPEP § 2143.01. In this case, the Examiner has not shown how the prior art suggested the desirability of the Nasir/Dixon/Dhar combination.

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In particular, the Examiner relies on Dhar to teach an aflatoxin oxime. However, the Examiner has not identified ***any*** motivation to combine Dhar with the other references and, thus, has given no reason why one of ordinary skill in the art would have derivativized aflatoxin to form an aflatoxin oxime and then conjugate it to a fluorophore to provide a fluorescent tracer for use in a fluorescence polarization assay. Indeed, one of ordinary skill in the art would ***not*** have been motivated to derivativize aflatoxin to form an aflatoxin oxime, as in Dhar, for at least the following three reasons:

(1) Dhar is directed to a ***heterogeneous*** assay, whereas fluorescence polarization assays are ***homogeneous***. Moreover, the claims are explicitly directed to homogeneous assays. Claim 1 recites "[a] homogenous assay ..." and claim 11 recites "in a homogeneous assay." As the Nasir reference makes clear, antibody-antigen interactions can differ depending on whether the assay is homogeneous or heterogeneous:

> In ELISA compounds adsorbed to the solid phase may have different affinities than in solution. The adsorbed antigens may denature with time [29], and at the solid phase steric hindrance might occur for larger molecules [30].

(Nasir, p. 191, col. 2). Thus, Nasir teaches away from reliance on the characteristics of heterogeneous assays, such as in Dhar.

(2) Dhar teaches the use of an enzyme label, which is a very different kind of label than a fluorophore. As a result, while Dhar may have suggested derivatizing aflatoxin to form an oxime in order to attach an enzyme label, Dhar would not have suggested to one of ordinary skill in the art using this derivatization approach in order to attach a fluorophore. This is especially apparent given point (3) below:

(3) The primary reference, Nasir, the only reference of the three that discusses fluorescence polarization assays, teaches conjugating a fluorophore to a mycotoxin antigen, ***not***

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to a derivative of a mycotoxin antigen: "A mycotoxin antigen of interest is labeled with a suitable fluorescent molecule (tracer)." (Nasir, p. 182, col. 1).

Thus, the Examiner's rationale supposes that one of ordinary skill in the art would have gone against the teaching in Nasir (the primary reference specific to fluorescence polarization) to fluorescently label the mycotoxin antigen, and would have instead used an oxime derivative as in Dhar -- even though Dhar is directed to a heterogeneous assay, says nothing about fluorescence polarization assays, and forms the oxime derivative in order to attach an enzyme label rather than a fluorophore. Clearly, the Examiner's rationale is far-fetched. Indeed, the Examiner has provided no explanation for why one of ordinary skill in the art would have taken these extraordinary steps.

Accordingly, the Examiner has failed to identify a motivation to combine the references and has failed to establish a *prima facie* case of obviousness.

c. No Prior Art Teaching Of A Reasonable Expectation Of Success

In order to establish a *prima facie* case of obviousness, the Examiner must also show that the prior art taught a reasonable expectation of success. *See* MPEP § 2143. In this case, the claims specify that the tracer (aflatoxin oxime conjugated to a fluorophore) has the special property of being able to bind to an antibody specific for aflatoxin "to produce a detectable change in fluorescence polarization." However, the Examiner has not shown that the prior art teaches a reasonable expectation of success with respect to achieving this special property.

As noted above, the Nasir reference teaches labeling the mycotoxin antigen with a fluorescent molecule. However, if a derivative of a mycotoxin antigen is fluorescently labeled instead, e.g., an aflatoxin oxime conjugated to a fluorophore, where is the prior art teaching that

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the product would have the special property of being able to bind to an antibody to produce a detectable change in fluorescence polarization?

The Examiner has failed to identify any such teaching in the prior art. The Examiner has not identified any prior art teaching that an aflatoxin oxime conjugated to a fluorophore would still be able to bind to an antibody specific for aflatoxin. Nor has the Examiner identified any prior art teaching that any binding would produce a detectable change in fluorescence polarization. In fact, Nasir teaches that even if binding occurs little polarization shift may be observed, due to a phenomenon called the "propeller effect." *See* Nasir, p. 180.

Accordingly, the Examiner has failed to identify a prior art teaching of a reasonable expectation of success and has failed to establish a *prima facie* case of obviousness.

4. Conclusion

Applicants submit that the present application is in condition for allowance and notice to that effect is hereby requested. Should the Examiner feel that further dialog would advance the subject application to issuance, the Examiner is invited to telephone the undersigned at any time at (312) 913-0001.

Respectfully submitted,

Date: December 10, 2004

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